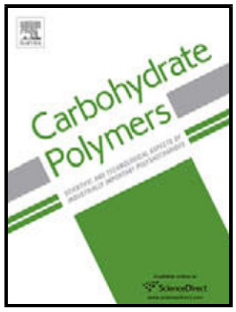

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INTER *vs.* INTRAGLYCOSIDIC ACETAL LINKAGES CONTROL SULFATION PATTERN IN SEMI-SYNTHETIC CHONDROITIN SULFATE

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Abstract

Microbial-sourced unsulfated chondroitin could be converted into chondroitin sulfate (CS) polysaccharide by a multi-step strategy relying upon benzylidenation and acetylation reactions as key-steps for its regioselective protection. By conducting the two reactions *one-* or *two-pots*, CSs with different sulfation patterns could be obtained at the end of the semi-synthesis. In particular, a CS polysaccharide possessing sulfate groups randomly distributed between positions 4 and 6 of *N*-acetyl-galactosamine (GalNAc) units could be obtained through the *two-pots* route, whereas the *one-pot* pathway allowed an additional sulfation at position 3 of some glucuronic acid (GlcA) units. This difference was ascribed to the stabilization of a labile interglycosidic benzylidene acetal involving positions *O*-3 and *O*-6 of some GlcA and GalNAc, respectively, when the benzylidene-acetylation reactions were conducted in a *one-pot* fashion. Isolation and characterization of a polysaccharide intermediate showing interglycosidic acetal moieties was accomplished.

Keywords: chondroitin sulfate; sulfation pattern; regioselective sulfation; interglycosidic linkage; acetal; benzylidene

1. Introduction

Glycosaminoglycans (GAGs) are biomacromolecules ubiquitously distributed in extracellular matrices and at cell surfaces, with a high biological significance. Chondroitin sulfate (CS), the most abundant GAG of the human body, is involved in a myriad of physiological and pathological processes, including central nervous system development, signal transduction, morphogenesis, wound healing, viral and bacterial infections (Yamada & Sugahara, 2008). From a structural point of view, CS is a highly negatively charged polysaccharide, constituted of glucuronic acid (GlcA) and *N*-acetyl-galactosamine (GalNAc), linked together through alternating β-(1→3) and β-(1→4) glycosidic bonds.

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